Insulin direct pancreatic progenitor cell differentiation via Pdx1 regulation

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Differentiation of early foregut endoderm into pancreatic endocrine and exocrine cells depends on a sequence of gene expression directed by various signals secreted from nearby tissue. Prior studies have shown that the pancreas is derived from Pdx1+ progenitor cells; however Pdx1 is turned off in pancreatic exocrine cells and α cells while maintained in β cells. Here, using zebrafish genetic knockdown, we showed that insulin secreted by early β cells can repress Pdx1 expression in pancreatic progenitor cells allowing them to differentiate to different pancreatic cell types. Knockdown of *insulin* gene severely impairs exocrine pancreas development. My results further demonstrate that inhibition of insulin signaling can induce pre-differentiation of Pdx1+ progenitor cells to β cells and Pdx1+ α cells. These Pdx1+ α cells can transdifferentiate to β cells following β cell ablation. Overall, these data represent the first in vivo evidence of local insulin signaling on pancreas development via regulation of Pdx1 expression.